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Ophthalmic Genetics: A New Synthesis

As INFECTIOUS DISEASES such as rubella have been brought under control with improved public health measures and immunizations, genetic factors have become increasingly important causes of both congenital and acquired eye diseases, particularly in the pediatric age group. Although accurate statistics are not available in the United States, it is estimated that at least 50% of new cases of legal blindness (20/200, or less than 20 degrees of peripheral vision) in the pediatric age group can be attributed to genetic causes; the economic and social consequences of this visual impairment are devastating. An ophthalmologist assumes a central role in identifying the cause of such visual handicaps and may assist pediatricians or geneticists in establishing a diagnosis in an otherwise perplexing patient. Referral is of particular importance in the detection of unilateral visual impairment, as a child with good vision in one eye may be asymptomatic. The eye is affected relatively early in the course of many genetic metabolic diseases and an ophthalmologist may be the first physician consulted. For example, patients who have Spielmeyer-Vogt disease, a lipopigment storage disorder, may have decreased central vision and ophthalmoscopic findings compatible with juvenile macular degeneration; progressive mental deterioration and visual impairment ensue. For some disorders, such as mannosidosis and Fabry's disease, the ocular manifestations are unique and diagnostic.

The hereditary bases of diseases that affect the eye include all three broad categories: chromosomal aberrations, single gene mutations consistent with Mendelian inheritance patterns and multifactorial inheritance. Some hereditary disorders that affect the eye have multiple genetic causes. The incidence of retinitis pigmentosa is about 1 in 3,000, much more common than would be expected from a disease caused by a single gene. Inheritance follows autosomal-dominant, autosomal-recessive and X-linked patterns. Although retinitis pigmentosa was thought to be a hereditary disease in all cases, a recent analysis of a large group of patients using segregation analysis, a complicated mathematical model, showed that some forms are not hereditary; the responsible environmental factors are not yet known.

The story of retinoblastoma has recently been unraveled. Strong evidence implicates a gene for this ocular malignancy on the short arm of chromosome 13 near the gene for esterase D, an enzyme that is unrelated to retinoblastoma. It is now believed that both the hereditary and the chromosomal forms of the disease are caused by an abnormality of the same gene. Neither the DNA sequence nor the biologic function of this oncogene has been identified.

The precedent for bringing a lawsuit for a wrongful birth has been set in the state of California by several cases that have been decided by the Supreme Court. Ophthalmologists and other physicians should consider the possibility of genetic factors in their visually handicapped patients; geneticists are well trained to relay information about hereditary disorders and congenital malformations without imposing value judgments.

J. BRONWYN BATEMAN, MD

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Laser Treatment for Glaucoma

THE OPHTHALMIC LASER was one of the earliest clinical applications of laser technology to medicine. Treatment of ocular disease primarily involved laser therapy for diseases of the macula, retinal tears and diabetic retinopathy. More recently, the argon laser has become a significant aid in the surgical treatment of both open-angle and closed-angle glaucoma. By using the laser, the number of patients requiring a conventional glaucoma operation has been reduced along with the associated complications, prolonged hospital care and inconvenience to patients and physicians.

Argon laser trabeculoplasty is the procedure used for open-angle glaucoma. Currently, it is the primary procedure of choice when the intraocular pressure cannot be adequately controlled medically. By placing small laser burns in the trabecular meshwork of the anterior chamber, the outflow facility of the eye increases and the intraocular pressure decreases. The 50 micron-sized burns are not full thickness, but cause stretching of the adjacent trabecular meshwork and enlarge the outflow channels. The surgical procedure is done on an outpatient basis, requires only topical anesthesia and is associated with minimal patient discomfort. Long-term follow-up is not available as the procedure first became a clinical research tool in the middle and late 1970s; however, three-year follow-up studies show an average decrease in intraocular pressure of 6 to 8 mm of mercury.

The optimal number of burns, their exact placement and the extent of the angle area to be treated are issues still under investigation.

For surgical management of cases of narrow (occludable) anterior chamber and narrow-angle glaucoma, argon laser iridotomy has replaced surgical iridectomy in all but the most difficult cases. This procedure is also done on an outpatient basis with topical anesthesia and minimal discomfort. In laser iridotomy, light is absorbed by the melanin pigment in the iris. The heat generated from the laser burn produces a full-thickness iris hole and allows aqueous humor to flow from the posterior to the anterior chamber of the eye. This relieves the pupillary block mechanism of narrow-angle glaucoma. After laser iridotomy the intraocular pressure is elevated temporarily from the dispersion of pigment into the anterior chamber. This elevation is usually mild and can be controlled medically. Some iris colors increase the difficulty of the procedure, particularly very light blue and very dark brown irides. Occasionally a full-thickness hole cannot be produced, requiring a repeat laser attempt or a conventional surgical iridectomy. Lens burn, mild iritis and corneal burns have been noted.

Argon laser trabeculoplasty and argon laser iridotomy are acceptable modes of surgical therapy, and have been valuable adjuncts in the clinical management of glaucoma.

E. LEIGH WILKINSON, MD
ROBERT E. CHRISTENSEN, MD

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Corneal Preservation

THE COLLECTION, evaluation and preservation of viable corneal tissue for purposes of transplantation are the major functions of a modern eye bank. Prospective donors are carefully screened by eye bank personnel for transmissible diseases or disqualifying ocular disease that would contraindicate their use as graft material. Tissue is then removed from a donor by enucleation of the whole globe or by excision of the cornea and a rim of sclera from the globe in situ within six hours after death.

Corneal tissue is evaluated by morphologic examination of the cornea with a slit-lamp biomicroscope or by using more recently developed specular microscopy for examination and counting of corneal endothelial cells.

Tissue preservation is necessary to allow for preparation of patients and transport of tissue and is accomplished by one of three methods: (1) moist-chamber storage of the whole globe, (2) intermediate cold storage in tissue culture medium and (3) long-term preservation in organ culture systems.

Corneas preserved as part of an intact globe in cold, moist-chamber storage must be used within 24 to 48 hours after death (short term). Storage of an excised cornea in modified tissue culture medium (McCarey-Kaufman [MK] medium) at 4°C extends tissue viability to 96 hours postmortem (intermediate term). More recently developed preservation of the delicate corneal endothelium in organ culture at 37°C has extended endothelial viability in storage to several weeks (long term). Most eye banks currently use intermediate-term preservation (MK medium).

Meticulous care to details of aseptic technique and preservation of endothelial integrity have enabled eye banks to provide excellent tissue to transplant surgeons and their patients. Medical standards for the qualifications of eye bank personnel, screening of appropriate donors, techniques of tissue handling and methods of corneal preservation have been determined by the Eye Bank Association of America.

MARK J. MANNIS, MD

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Extended-Wear Lenses and Corneal Infections

EXTENDED-WEAR soft contact lenses have been approved for use in both myopic and hyperopic patients for several years. While some of the initial concerns involved the ability of the cornea to metabolically tolerate these lenses over longer periods, this has not proved to be of major consequence. Rather, more significant problems have occurred in two other areas—lens maintenance and infections. Some patients must remove their lenses to eliminate films and deposits. Unfortunately this is especially true in older patients who would benefit most from limited handling. While this problem provides a certain inconvenience, it is of no serious medical consequence.

Infection, however, may be the cause of permanent visual loss. It has been shown that merely having an extended-wear lens in place does not seem to change the normal bacterial flora of the eye. Nevertheless, corneal ulcers can and do occur, resulting in corneal scarring. Whereas these infections are uncommon, they occur when least expected and without warning. One would think that decreased handling would result in reduced incidences of infection, but this is apparently not the case. They are probably related to oxygen compromise. Continual administration of antibiotic drops is not justified, although hygiene is important to maintain. It is vital, however, that a red eye in a patient using extended-wear lenses be reported to that patient's ophthalmologist immediately.

RICHARD ELANDER, MD

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YAG Laser Posterior Capsulotomy

CATARACT OPERATIONS and intraocular lens implantation have changed dramatically in the past decade. Extracapsular surgical treatment in which the posterior capsule of the lens is preserved is popular because of the possible benefits of improved lens fixation and reduced risk of retinal detachment and cystoid macular edema. In 30% to 50% of cases, the posterior capsule opacifies in the years following a cataract operation. Until recently treatment of opacified capsules was limited to invasive procedures to open the membrane.

Working simultaneously and independently, Aron-